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Patterns of care and outcomes for elderly patients with metastatic colorectal cancer in Australia[☆]



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ABSTRACT

Objectives: The elderly accounts for a large proportion of patients with metastatic colorectal cancer (mCRC). This study reviews patterns of care and outcomes for elderly patients with mCRC in the community setting.

Materials and Methods: Elderly patients (≥ 65 years) with mCRC on the TRACC (Treatment of Recurrent and Advanced Colorectal Cancer) registry were identified. Treatment, bevacizumab-related adverse events, and overall survival (OS) were analysed by age cohorts, comparing those aged 65–74 vs. 75–84 vs. ≥ 85 years and correlated with potential prognostic factors. Factors affecting chemotherapy and bevacizumab administration were analysed using logistic regression analysis.

Results: Of 1439 patients, 363, 352, and 106 were aged 65–74, 75–84, and ≥ 85 years, respectively. 584 (71%) patients received first-line chemotherapy, with chemotherapy use declining with advancing age (84%, 69%, and 34% in 65–74-, 75–84- and ≥ 85 -year-olds, respectively). Seven (10%) patients aged ≥ 85 years were not treated with chemotherapy on the basis of age alone. Only 10 of 36 very elderly patients who received chemotherapy also received bevacizumab. Factors affecting bevacizumab administration included age, treatment location, and comorbidities. There was no impact of age on bevacizumab-related adverse events. Resection of metastatic disease occurred in 173 (21%) patients overall, with rates declining with age (26% vs. 21% vs. 6%).

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Conclusion: Chemotherapy usage and resection of metastatic disease decline with advancing age. A minority of patients are not treated with systemic therapy due to advanced age alone. Our cohort suggests underutilisation of bevacizumab in older patients, but where given, toxicity rates did not increase with age.

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1. Introduction

Cancer is predominantly an age-related disease, with approximately 60% of new cancer diagnoses and 70% of all cancer deaths occurring in those aged over 65 years.¹ This age-related risk is illustrated in the epidemiology of colorectal cancer (CRC) in Australia, where the average age at diagnosis is 69.3 years, with CRC accounting for 9.3% of all cancer deaths.²

There is a paucity of safety and efficacy data in elderly patients due to underrepresentation in clinical trials, where the median age of patients enrolled is typically 60–65 years. This is partly due to a reluctance of investigators to enrol elderly patients onto clinical trials, along with stringent eligibility criteria, such that elderly patients are excluded based on poor functional status, major organ dysfunction, cognition, or even chronological age alone.³ There is also a paucity of data related to the surgical approach to elderly patients, both for those with an intact primary and those with resectable metastatic disease.

Previous studies suggest that a significant proportion of elderly patients in routine practice do not receive treatment despite evidence suggesting that current combination chemotherapy regimens for metastatic CRC (mCRC) are equally tolerable for older persons enrolled on clinical trials, with similar treatment benefits observed compared to younger patients.⁴ Notably, however, studies enrolling only elderly patients^{5,6} have not been able to confirm these findings, raising questions about the role of upfront combination chemotherapy in older patients.

The addition of bevacizumab to chemotherapy in the treatment of mCRC has resulted in clinically significant improvements in progression-free and overall survival (OS),⁷ with evidence suggesting a similar clinical benefit across all age groups,^{8,9} including studies only enrolling elderly patients.¹⁰ Bevacizumab is generally well tolerated, although increased toxicity rates, particularly thromboembolic events, have been reported among older patients.^{9–11}

The purpose of this study was to review treatment patterns and outcomes in elderly patients with mCRC in a non-clinical trial setting, according to three age subgroups: 65–74, 75–84, and ≥ 85 years. Of particular interest were the impact of performance status and comorbidity on clinician decision-making. Along with this, the reason for any elderly patient not receiving active treatment was prospectively recorded. The findings of this study reflect current Australian practice in managing elderly patients with mCRC.

2. Materials and Methods

Secondary analysis of prospectively collected data of patients with mCRC aged ≥ 65 years identified from the TRACC

(Treatment of Recurrent and Advanced Colorectal Cancer) registry.¹² This database was initiated between BioGrid Australia and Roche Australia in 2009 to prospectively collect data for consecutive patients with newly diagnosed mCRC, including those who do not receive active therapy. Data were collected by clinicians at the point-of-care and entered into local research repositories at the individual institutions. Comorbidities were recorded at initial review; Eastern Cooperative Oncology Group performance status (ECOG PS) was recorded at initial review and at commencement of chemotherapy (where given).

Clinicians were asked to record treatment discussion, including treatment options discussed and reason for treatment recommendation where chemotherapy was not given. Pre-defined reasons for not offering chemotherapy were recorded in checkbox format, with more than one reason allowed.

Clinicians were encouraged to record toxicities continuously but were also prompted monthly regarding bevacizumab-related toxicities. All grades of toxicities were allowed, but only the worst grade was recorded. Toxicities were assessed using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. Follow-up was captured until 14 August 2014, with median follow-up of 26.4 months.

3. Statistical Analysis

In this analysis, patients with newly diagnosed mCRC, including those who had prior treatment for an early stage CRC, were enrolled from 1 July 2009 to 30 June 2014. The cohort of elderly patients was analysed according to three age subgroups: 65–74, 75–84, and ≥ 85 years, to explore differences in clinicopathologic features, treatment delivery, adverse events, and outcomes.

Descriptive statistics and the chi-square test were used to analyse differences in characteristics between the age groups. Univariate and multivariate logistic regression analysis was used to explore factors associated with chemotherapy and bevacizumab administration.

Kaplan-Meier estimates of overall survival were calculated separately for the different patient age groups and compared using the log-rank test where P-values of ≤ 0.05 were considered significant. Cox regression analysis was performed to analyse the effect of age, sex, treatment location, ECOG PS, Charlson comorbidity index (CCI) score,¹³ and resection of primary tumour on overall survival.

All analyses were carried out using SAS 9.4 Enterprise Guide V6.1 and GraphPad Prism V6.01 (GraphPad Software Inc., California, USA) analysis tools.

Approval for the study was obtained from the research and ethics committees of the participating institutions.

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